SUBCORTICAL BAND HETEROTOPIA SYNDROME IN CHILDREN – COMPARISON OF TWO CASE REPORTS

Smaranda Nita[1], Magdalena Sandu[2], Raluca Teleanu[1,2]

[1]Department of Pediatric Neurology, "Dr. Victor Gomoiu" Children's Hospital, Bucharest

[2]"Carol Davila" University of Medicine and Pharmacy, Bucharest

ABSTRACT

This article aims to present the cases of two pediatric patients with Subcortical Band Heterotopia, monitored in our clinic over a period of one year with respect to seizure frequency and cognitive as well as behavioral evolution. While one of the patients was born at 32 weeks and had a delay in reaching the normal develomental milestones, the second patient had no significant history of psychomotor delay. Both patients showed epileptic seizures, one of them evolving to intractable epilepsy, mild cognitive decline and behavioral problems, while the other presented a wide seizure-free interval and no cognitive impairment. Finally, we would like to emphasize that in a child with epilepsy and psychomotor delay, with an evocative EEG, cortical development disorders should be considered and magnetic resonance imaging (MRI) should be carried out.

Key words: Subcortical Band Heterotopia, epilepsy, cognitive impairment, children

INTRODUCTION

Subcortical Band Heterotopia (SBH) or "Double Cortex" syndrome is a neuron migration disorder predominately affecting females, associated with a mutation of the XLIS gene located on Xq22.3-23 chromosome, characterized by an imagistic discernible band-like appearance of heterotopic neurons separated from the normal cortex by a layer of white matter.

This aspect results from an impairment of neuronal migration, a cortical development process which takes place during the third to fifth months of gestation. Disruption of the normal process of neuronal migration results in a recognizable group of malformations known as "neuronal migration disorders". Due to recent advances in molecular biology, genetics and imaging studies, efforts have been made to give rise to a classification of these disorders which can best reflect the increasing knowledge of cortical development and the mechanisms of its disorders. According to Barkovich, Guerrini et al (1), SBH is classified in the II.B lissencephaly spectrum, comprising of widespread abnormal transmantle migration malformations.

The clinical manifestations in children with neuronal migration disorders consist of epileptic seizures, most of the times progressing towards drug-resistant epilepsy and mental retardation. Moreover, children with SBH might demonstrate cognitive as well as behavioural problems (2). The use of magnetic resonance imaging (MRI) in investigating children with this symptomatology has led to an increase in the frequency of diagnosing neuronal migration disorders.

We present the cases of two female patients kept under observation in our clinic over a period of one year, through clinical, electroencephalografic and psychological assessments, both displaying an imagistical aspect of "double cortex" syndrome and a clinical picture consisting of seizures and mild

Author for correspondence:
Assoc. Prof. Raluca Ioana Teleanu MD, PhD, "Dr. V. Gomoiu" Children's Hospital, 21 Basarabia Bd, Bucharest
e-mail: ralucate@gmail.com

mental retardation, however with different characteristics.

CASE REPORTS

Case I

History

The first case is of a 17 year-old female patient who was admitted to our clinic for recurrent drug resistant epileptic seizures and lowering of school performance. The seizures had started around the age of 4, at that time their aspect being of tonic seizures with a partial onset and secondary generalization, predominantly occuring during sleep, with a frequency of about one episode per week. Subsequently, the frequency of the seizures rose to up to 20-25 episodes per night and their aspect became polymorphic, the child also manifesting generalized tonic-clonic seizures, as well as "drop-attacks", during the day. Various antiepileptic drug (AED) schemes were employed, consisting in valproic acid, phenitoin, phenobarbital, lamotrigine, clonazepam, levetiracetam, topiramate, ethosuximide, diazepam, oxcarbazepine, without a significant lowering in the frequency of seizures. At the same time, parents reported a lowering of the child's school performance.

Clinical and paraclinical examinations

Her personal and family history were unremarkable. The physical and neurological examinations were normal, except for bradylalia and bradyphychia. The EEG recording during wakefulness showed a background polymorphic activity in the alpha frequency range with aperiodic spike-and-wave discharges, with a higher amplitude over the right hemisphere (Figure 1).

The cerebral MRI showed the characteristic aspect of "double cortex" syndrome: a diffuse band of dark matter situated between the lateral ventricles and the cortical surface, separated from the normal cortex by a thin layer of white matter (Figure 2).

The psychological examination revealed a mild cognitive impairment and bradylalia, as well as behavioral abnormalities.

Treatment and evolution

The patient is currently on Valproic Acid (1125 mg/day), Topiramate (275 mg/day) and Clobazam (17,5 mg/day). She keeps having seizures, however with a lower frequency of about 2-3 episodes per week, mainly diurnal, characterized by loss of consciousness and "head drop", lasting for 3-5 seconds, followed by postictal confusion. Psychologically,

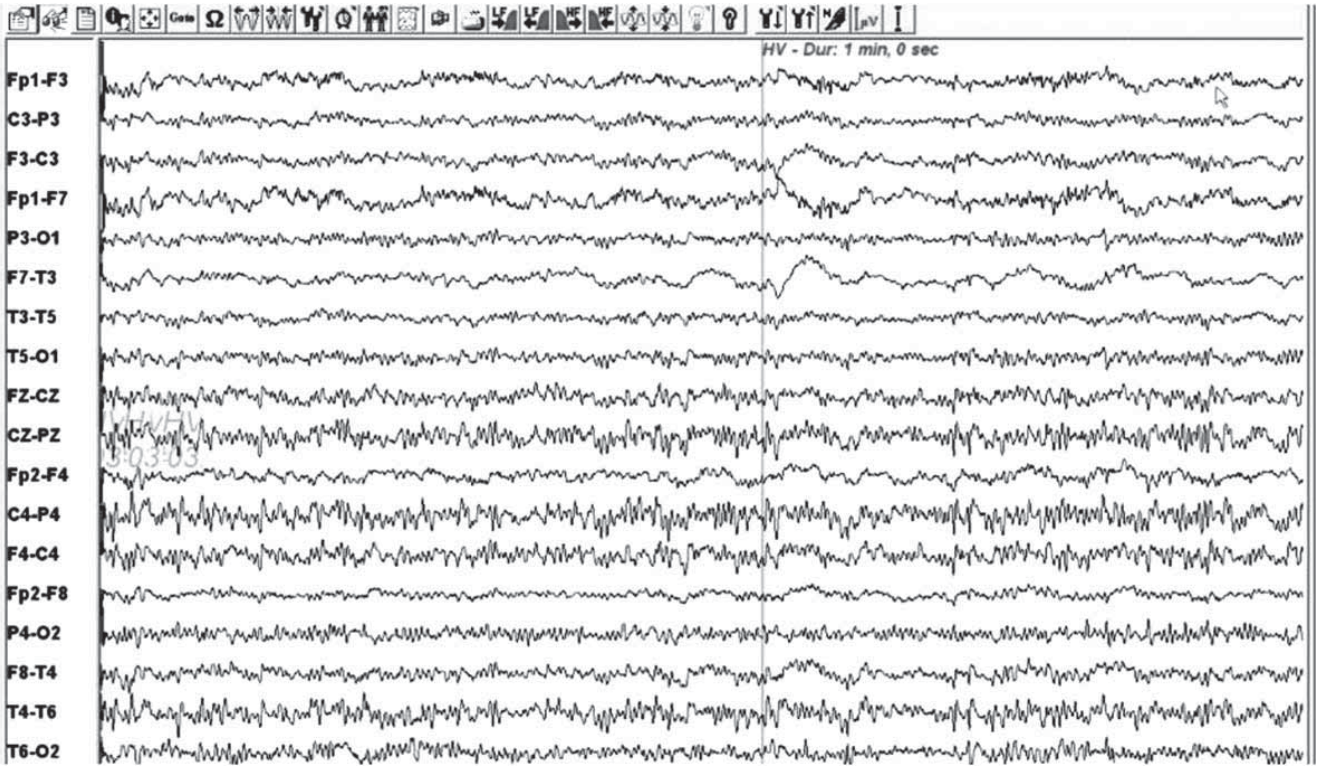

FIGURE 1. *Interictal EEG during wakefulness – inconsistent left to right asymmetry with background polymorphic activity in the alpha frequency range; aperiodic spike-and-wave discharges with a higher amplitude over the right hemisphere. Sensitivity: 150 microvolts*

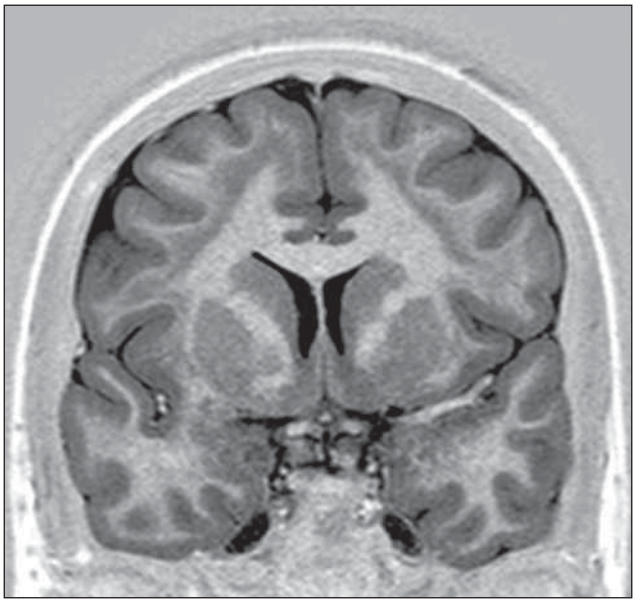

FIGURE 2. *T1-weighted Coronal Cerebral MRI – „double cortex" aspect*

the same pattern has been noted over time. Her EEG at the moment is uncharacteristic, displaying the same background polymorphic activity in the alpha frequency range, with occasional and aperiodic spike- and – wave discharges.

Case II

History

The second case is that of a 9 year – old female patient, who was initially admitted to our clinic for two consecutive right-sided partial seizures. The seizure onset was at the age of five, when, according to the description provided by the family, she developed a left sided partial seizure with secondary generalization and progression to status epilepticus. While no significant familial history has been noted, the child was born at 32 weeks and had a mild psychomotor delay accompanied by speech disturbances.

Clinical and paraclinical examinations

Upon arrival at our clinic, her physical and neurological examinations were within normal limits, except for dyslalia. The EEG during wakefulness showed a relatively syncronous activity in the alpha frequency range, with superimposed periodic suggestive aspects of "high amplitude, fast activity", an electroencephalografic pattern previously noted occasionally in connection to neuronal migration disorders (Figure 3).

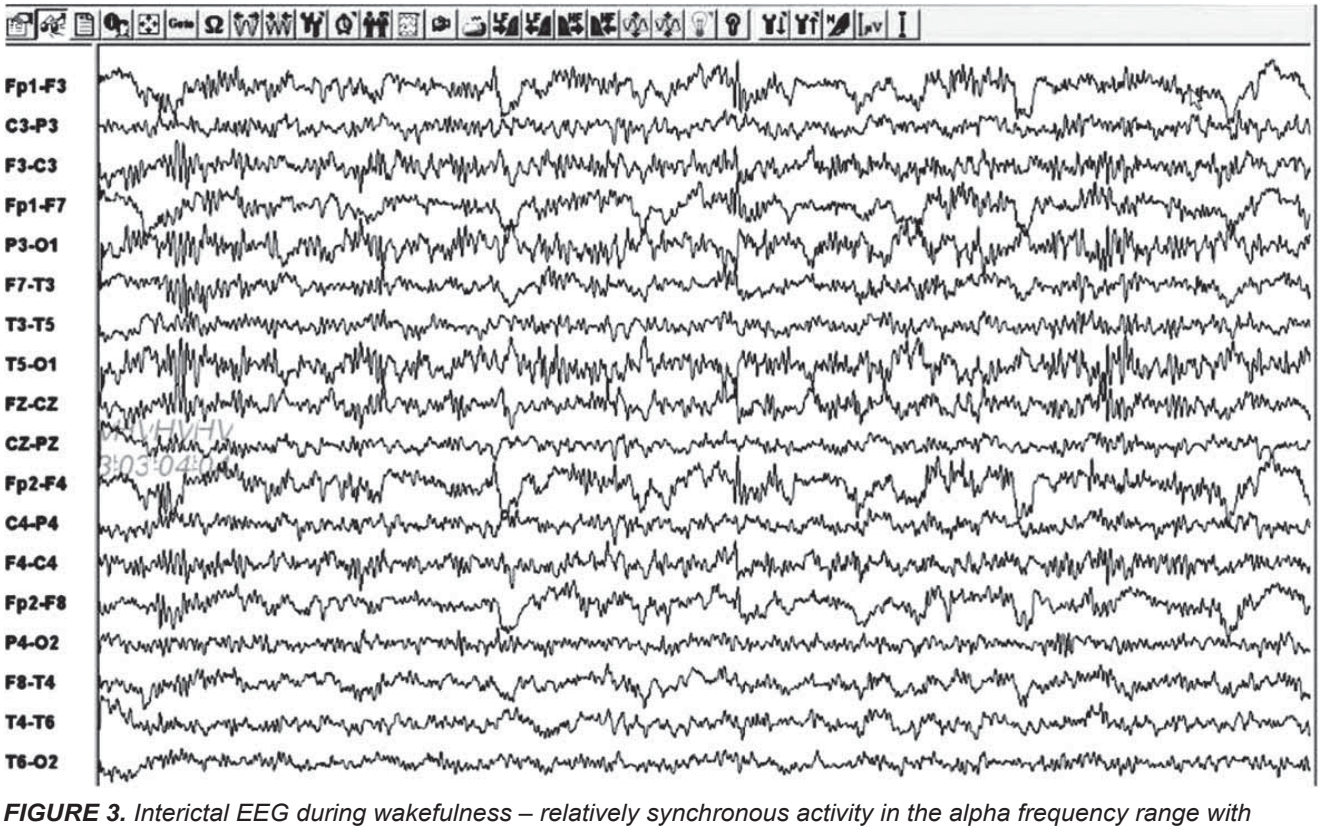

FIGURE 3. *Interictal EEG during wakefulness – relatively synchronous activity in the alpha frequency range with superimposed periodic aspects of "high amplitude, fast activity". Sensitivity: 150 microvolts*

The cerebral MRI revealed the same aspect of "double cortex" mentioned above (Figure 4).

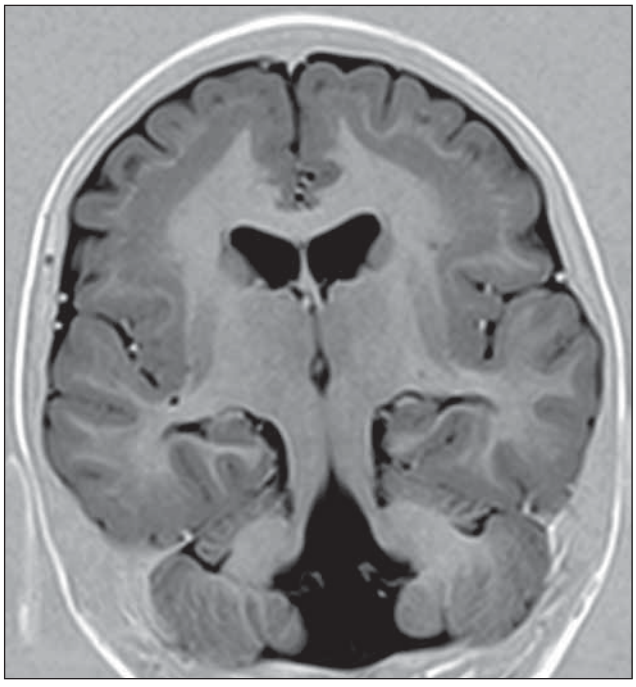

FIGURE 4. *T1 – weighted Coronal Cerebral MRI – „double cortex" aspect*

The psychological examination showed a mild psychomotor delay and a bradylalic and dyslalic speech.

Treatment and evolution

The patient has been on treatment with Valproic Acid, currently at 25 mg/kg/day, with a favorable evolution regarding seizures, presenting only one additional short seizure throughout the period of one year. Her mental abilities have maintained the same level and she is undergoing speech therapy. The EEG aspect has not changed significantly over time.

CONCLUSIONS

The cases presented in this article illustrate the fact that neuronal migration disorders can have polymorphic clinical as well as electroencephalografic aspects, both our patients displaying epileptic seizures but with different forms and frequency and uncharacteristic EEG patterns. The investigation which prompted the diagnosis was the cerebral MRI, which revealed the characteristic aspect of this cortical malformation. Because of the diffuse involvement of the brain, in both cases the treatment was aimed at lowering the frequency of the seizures and the psychological profiles of the patients have been monitored, in order to account for possible changes along the course of evolution and treatment.

REFERENCES

1. **Barkovich A.J.** A developmental and genetic classification for malformations of cortical development: update 2012, *Brain*, 2012
2. **Spencer – Smith M.** Neuropsychological profile of children with subcortical band heterotopia, *Developmental Medicine and Child Neurology*, 2009
3. **Kerjan G., Gleeson J.** Moving neurons back into place, *Nat Med.*, 2009 January; 15(1): 17–18
4. **Dericioglu N.** Ictal/Interictal EEG Patterns and Functional Neuroimaging Findings in Subcortical Band Heterotopia: Report of Three cases and Review of Literature, *Clinical EEG and Neuroscience;* Jan 2008; 39, 1
5. **Jacobs R.** Neuropsychological profile of a 9-year-old child with subcortical band heterotopia or 'double cortex, *Developmental Medicine and Child Neurology;* Sep 2001; 43, 9
6. **Matsumoto N.** Mutation analysis of the *DCX* gene and genotype/phenotype correlation in subcortical band heterotopia, *European Journal of Human Genetics*, 2001; 9, 5–12
7. **Beaudoin B.S.** Brief Report: The Impact of Subcortical Band Heterotopia and Associated Complications on the Neuropsychological Functioning of a 13-year-old Child, *J Autism Dev Disord*, 2007; 37:983–992